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Docket No. 1662/49502  
JUL 12 2002

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT : SINGER ET AL.  
SERIAL NO. : 09/552,485  
FILING DATE : April 18, 2000  
FOR : NOVEL SYNTHESIS AND CRYSTALLIZATION OF  
PIPERAZINE RING-CONTAINING COMPOUNDS  
GROUP ART UNIT : 1624  
EXAMINER : K. Habte

**Request for Interference Between Applications Pursuant to 37 CFR § 1.604**

ASSISTANT COMMISSIONER FOR  
PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Sir:

Pursuant to 37 CFR § 1.604, Applicants respectfully request that an interference be declared between the above-captioned application and U.S. Patent Application Serial No. 09/697,329 ("the '329 application"), filed October 27, 2000. The information required by 37 CFR § 1.604(a) is set forth below.

(1) Proposed Count

Applicants propose the following three alternative counts.

Count 1

A process for preparing a crystalline adduct of mirtazapine and water comprising the steps of:

- i) crystallizing mirtazapine from a solution comprising water;
- ii) recovering crystallized mirtazapine; and
- iii) drying the crystallized mirtazapine until the crystallized mirtazapine contains up to about 3 weight percent water.

**Count 2**

A crystallized adduct of mirtazapine and water prepared by:

- i) crystallizing mirtazapine from a solution comprising water;
- ii) recovering crystallized mirtazapine; and
- iii) drying the crystallized mirtazapine until the crystallized mirtazapine contains up to about 3 weight percent water.

**Count 3**

A crystalline adduct of mirtazapine and water containing up to about three weight percent water.

As discussed below, Applicants do not know the exact claim language recited in the claims currently pending in the '329 application. Accordingly, Applicants offer the three foregoing counts as alternatives. Applicants do not necessarily contend that the three counts reflect "separate patentable inventions," as defined in 37 CFR § 1.601(n). Alternatively, Applicants would consider any count(s) that might be proposed by the Examiner.

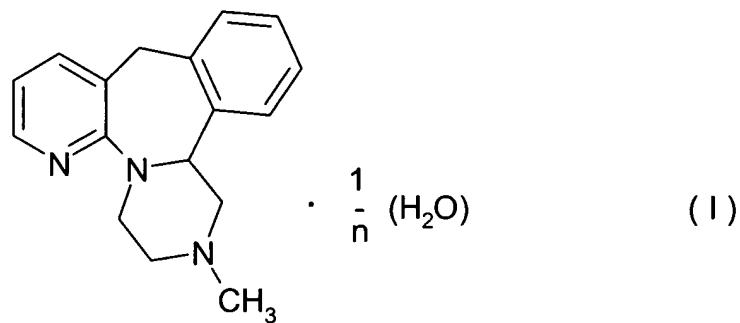
In its Response to the Final Office Action dated March 13, 2002 (filed concurrently herewith), Applicants respectfully requested reconsideration of the above-identified application in view of the amendments and remarks made therein. New independent claim 46 corresponds exactly to count 1. Dependant claims 47-53 correspond substantially to count 1. Independent claim 37 corresponds exactly to count 2. Dependant claims 38-41 correspond substantially to count 2. Pending independent claim 30 corresponds exactly to count 3. Dependant claims 31-35 correspond substantially to count 3. Some of these claims may correspond substantially to additional counts. For the reasons set forth in the Response, Applicants submit that all of the claims corresponding to one or more of the counts are in condition for allowance.

**(2) Corresponding Claims in the '329 Application**

The following claims are translations of claims 7 and 8 that were presented, *inter alia*, in published PCT Application WO 01/38330 (the original Japanese-language publication and an uncertified translation is attached as Appendix A for convenient reference by the Examiner). Since the claim numbers of the '329 application are unknown to Applicants, the following claims

are referred to as "the hydrate claim of the '329 application" and "the method claim of the '329 application," respectively.

7. Crystals of mirtazapine hydrate shown in formula (1) (in which n represents an integer 1 - 5):



8. A method for the production of crystalline mirtazapine hydrate the special feature of which is the crystallization of crude mirtazapine using water-soluble polar organic solvents and water.

The hydrate claim of the '329 application corresponds substantially to Count 2 and Count 3 because for one or more values of n, the recited hydrate contains up to about 3 weight percent water.<sup>1</sup> Example 4 of the corresponding PCT application, for instance, states that one embodiment of the invention is a hydrate containing 2.8% by weight water. The method claim corresponds substantially to Count 1 because Count 1 anticipates the method claim.

(3) Explanation For Why An Interference Should Be Declared

The hydrate claim of the '329 application claims the same patentable invention, as defined in 37 CFR § 1.601(n), as Applicants' claimed invention because one or more claims of the '329 application are anticipated and/or obvious in view of Applicants' claimed invention, and one or more claims of the Applicants' pending application are anticipated and/or obvious in view of one

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<sup>1</sup>For example, when n = 5, one mole of this hydrate would contain 0.2 mol water (3.6 g) and 1.0 mol mirtazapine (265 g), which is 1.3% by weight water.

or more claims of the '329 application.

The '329 application discloses and claims a mirtazapine hydrate intermediate, and its manufacture, for the preparation of anhydrous mirtazapine. The mirtazapine hydrate is manufactured according to the steps recited in Count 1 and Count 2 and is therefore anticipated by either of these two counts. Consider, for instance, Example 1 in the translated PCT application corresponding to the '329 application. In this Example, mirtazapine hydrate containing 2.3% by weight water was prepared by dissolving crude mirtazapine in ethanol, adding water dropwise to the ethanol solution, cooling the solution to form crystals, and drying the crystals at 70 °C. The claimed mirtazapine hydrate is anticipated by Count 2 and Count 3 because, as explained above, the claimed mirtazapine hydrate contains up to about 3% by weight water. Similarly, one or more of Applicants' claims corresponding to the counts would be anticipated and/or obvious in view of one or more of the claims of the '329 application.

As further evidence that the mirtazapine hydrate of the '329 application may overlap with Applicants' claimed adduct is that the '329 application discloses a hemihydrate of mirtazapine having similar physical properties as Applicants' claimed adduct. See Second Aronhime Declaration (Appendix B).<sup>2</sup>

#### V. Conclusion

For the foregoing reasons, Applicants respectfully request that an interference be declared between the above-captioned application and U.S. Patent Application Serial No. 09/697,329 pursuant to 37 CFR § 1.604.

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<sup>2</sup>The attached declaration is unsigned; a signed copy shall be forwarded to the Patent Office shortly.

The Examiner is invited to contact the undersigned attorney regarding any matter concerning this Request or the pending application. The Commissioner is authorized to charge or debit any underpayment or overpayment to Deposit Account 11-0600.

Respectfully submitted,

Date: 7/11/02



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